

increasing the relative percentage of said population of nucleic acids of interest within a mixed population of nucleic acids, wherein said mixed population comprises a plurality of nucleic acid sequences, comprising:

B9 (a) contacting a nucleic acid sample with a nucleic acid bait molecule, wherein said nucleic acid sample comprises said nucleic acids of interest and at least one unwanted target sequence and wherein said bait molecule binds specifically to said unwanted target sequence, but not to said nucleic acids of interest, under such conditions as to allow for the formation of a bait:target complex;

(b) digesting the unwanted target sequence in the bait:target complex thereby resulting in an increase in the relative percentage of said nucleic acids of interest within said mixed population of nucleic acids; fragmenting said nucleic acids of interest to produce fragments; and adding a label to the fragments.

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B10 6. The method of claim 1 wherein said nucleic acids of interest are messenger RNA (mRNA).

7. The method of claim 1 wherein said unwanted target sequence is rRNA or tRNA.

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B11 9. The method of claim 1 wherein said unwanted target sequence is 23S RNA.

10. The method of claim 1 wherein said unwanted target sequence is 16S RNA.

11. The method of claim 1 wherein said bait molecule is generated from a population of nucleic acids other than the nucleic acid of interest.

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B12 14. The method of claim 1 wherein said bait molecule is synthesized by hybridizing a primer to said unwanted RNA target sequence and extending said primer by reverse transcriptase using said target sequence as a template.

15. The method of claim 1 wherein the nucleic acid sample is an RNA sample, the bait molecule is DNA, and the bait:target complex is a DNA:RNA hybrid.

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B13 17. The method of claim 1 wherein said bait molecule is attached to a solid substrate.

B14 20. The method of claim 1 wherein said bait molecule is modified to comprise a selectable element.

B15 22. The method of claim 20 further comprising the step of exposing said bait:target complex to a reagent that binds said selectable element to form a reagent:bait:target complex prior to the step of digesting the unwanted target sequence.

23. The method of claim 22 wherein the reagent that binds said selectable element is selected from the group consisting of: a nucleic acid sequence, a ligand, a receptor, an antibody, a haptenic group, an antigen, an enzyme or an enzyme inhibitor.

B16 25. The method of claim 22 wherein said selectable element is biotin and said reagent that binds said selectable element is streptavidin.

26. The method of claim 22 further comprising separating said reagent:bait:target complex from said mixed population prior to the step of digesting the unwanted target sequence..

B17 29. The method of claim 15 wherein the step of digesting said unwanted target sequence comprises exposing said DNA:RNA hybrid to a reagent which digests RNA in a DNA:RNA hybrid and digesting said unwanted target sequence and wherein said reagent is RNase H.

B18 31. The method of claim 1 further comprising the step of removing the bait molecule after digesting the target sequence in said bait: target complex

32. The method of claim 29 further comprising the step of removing any remaining DNA bait molecules after said unwanted target sequence is removed.

33. The method of claim 32 wherein said step of removing said DNA bait molecules is accomplished by digestion with DNase I.

38. The method of claim 1 wherein said label is a biotin.
39. The method of claim 1 wherein said label is a polyethylene oxide-Iodoacetyl Biotin.
40. The method of claim 1 wherein the label is attached to the 5' ends of said fragments.
41. The method of claim 1 wherein after said step of fragmenting, said 5' ends of said fragments are chemically modified.
42. The method of claim 41 wherein the 5' ends of said fragments are chemically modified by  $\gamma$ -S-ATP and T4 kinase.
43. The method of claim 41 wherein said chemical modification results in the addition of a thiol group to the 5' end of said fragments.
44. The method of claim 43 wherein said detectable signal moiety is polyethylene oxide-Iodoacetyl Biotin.

#### REMARKS

##### ***Informalities***

The specification has been amended to replace the colons (:) with the symbol for micro,  $\mu$ , where appropriate. Claim 6 has been amended to place the period outside of the parentheses and claim 42 has been amended to replace the left parentheses with the  $\gamma$  symbol. Applicants would like to thank the Examiner for pointing out these errors.

##### ***Rejection under 35 USC §112, first paragraph***

Applicants have amended claim 1 to include the limitation that the bait molecules are nucleic acid bait molecules as suggested by the Examiner in paragraph 4.